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PROPHYLAXIS IN VON WILLEBRAND DISEASE PATIENTS

Von Willebrand disease (VWD) is the most common inherited bleeding disorder resulting from a deficiency or dysfunction of von Willebrand factor (VWF). VWF has an integral role in hemostasis because it binds to and stabilizes FVIII as well as facilitating platelet adhesion to the injured endothelium. VWD has been characterized into three types: type 1, the most common, caused by a partial quantitative deficiency of VWF; type 2 which is observed in approximately 20% of cases and results from VWF dysfunction due to qualitative abnormalities; type 2 VWD has been further subdivided into four subtypes: while type 2A is characterized by a loss of high-molecular-weight VWF, type 2B results from a change in the VWF structure leading to an increased affinity to platelets. Type 2M is caused by a reduced interaction of VWF with platelets, and type 2N results from reduced binding capacity of VWF to FVIII. Type 3, the rarest form, occurs in less than 1% of cases and is due to a virtual absence of VWF.

Individuals affected benefit from care in a comprehensive bleeding disorders program. The two main treatments are desmopressin (1-deamino-8-D-arginine vasopressin [DDAVP]) and clotting factor concentrates (recombinant and plasma-derived) containing both VWF and FVIII (VWF/FVIII concentrate). Indirect hemostatic treatments that can reduce symptoms include fibrinolytic inhibitors; hormones for menorrhagia are also beneficial. Individuals with VWD should receive prompt treatment for severe bleeding episodes. Pregnant women with VWD are at increased risk for bleeding complications at or following childbirth. The major symptoms that are present in patients involve mucocutaneous and gastrointestinal bleeding, including epistaxis, easy bruising, as well as provoked bleeding due to injury, surgery, and other invasive procedures, especially dental work. Patients with severe forms of VWD may have frequent haemarthroses, some patients have recurrent gastrointestinal bleeding, often without lesions in the gastrointestinal tract, and need treatment every day or every other day. Finally, there are children who frequently have epistaxis and severely enough to cause anaemia. In these frequent and severe bleeders, the optimal therapy may be regular prophylaxis with VWF/FVIII concentrates rather than on-demand treatment on the occasion of bleeding episodes. A prospective, observational, national post-marketing study, which enrolled patients of all ages and VWD types, was conducted in France from 2004 to 2009. Patients were observed for up to 3 years and treated with a pure VWF concentrate (Wilfactin®) on one or more occasions. Efficacy was assessed for each major event. This study showed that Wilfactin allowed a very high efficacy response in surgery to prevent perioperative bleedings, in curative treatment, and in long-term prophylaxis with no remarkable safety signals. In particular, there were no thrombotic events, even in high-risk patients. In less than half of the cases a priming dose of factor VIII had to be given to obtain the rapid increase in FVIII:C needed in some situations. Wilfactin provided a sound basis for effective and tailored patient treatment across a range of clinical settings.